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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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23280	7590	10/20/2003		
DAVIDSON, DAVIDSON & KAPPEL, LLC 485 SEVENTH AVENUE, 14TH FLOOR NEW YORK, NY 10018				
			EXAMINER GOLLAMUDI, SHARMILA S	
			ART UNIT 1616	PAPER NUMBER 20

DATE MAILED: 10/20/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

Application No.

09/435,576

Applicant(s)

CHEN ET AL.

Examiner

Sharmila S. Gollamudi

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on 22 July 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 1-13, 18, 19, 21, 22, 25-29, 31-54, 57-71 and 76-81 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-13, 18-19, 21-22, 25-29, 31-54, 57-71, and 76-81 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

## Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

## Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_\_.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

### **DETAILED ACTION**

Receipt of Extension of time and Amendment A received on July 22, 2003 is acknowledged. Claims **1-13, 18-19, 21-22, 25-29, 31-54, 57-71, and 76-81** are pending in this application. Claims 14-17, 20, 23-24, 30, 55-56, and 72-78 stand cancelled.

#### ***Claim Rejections - 35 USC § 112***

Rejection of claims 1-75 under 35 U.S.C. 112, first paragraph, as based on a disclosure which is not enabling is withdrawn.

Rejection of 14, 23-24, 30, 55-56, and 58 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn.

#### ***Claim Rejections - 35 USC § 103***

**Claims 1-13, 18-19, 21-22, 25-29, 31-54, 57-71, and 76-81 are rejected under 35 U.S.C. 103(a) as being unpatentable over Alberts et al (4,997,658) or Cheng et al (Pharmaceutical Research) in view of Oshlack et al (5,472,712).**

Alberts teaches a method of lowering plasma cholesterol levels. The method includes administering to a subject a time-controlled drug-delivery device containing an HMG-CoA reductase inhibitor (lovastatin). Alberts discloses that using a sustained or controlled release provides for a single dose to yield an equivalent or improved effect while lowering the peak drug plasma levels (col. 1, lines 39-50). By lowering the amount of plasma concentration in the blood, the potential side effects of the drug are reduced. The controlled release is over a 6 to 24 hour period (col. 2, line 63). Alberts discloses that this controlled release can be achieved by a variety of procedures known to those

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skilled in the art. The procedures suitable for the invention are diffusion-controlled systems, osmotic devices, dissolution controlled matrices, and erodible/degradable matrices (col. 3, lines 1-2).

Cheng et al teach the efficacy of a sustained/controlled release dosage form for the delivery of lovastatin or simvastatin. Cheng et al teach lowering cholesterol level. Cheng teaches the lower plasma concentrations of the instant drugs results in equal or better therapeutic efficacy. The instant Cmax is taught (figures).

Alberts or Cheng et al do not specify the formulation for the control release device.

Oshlack et al teach a stabilized control release formulation. The formulation can include various pharmaceuticals, which can provide a therapeutic effect for 12 to 24 hours (col. 4 and col. 5, lines 20). Oshlack provides a once a day administration and teaches Cmax and Tmax of the drug of choice (examples). Oshlack teaches a coating in order to obtain the desired release profiles (Note figures) and manipulation of the release profile by adding release-modifying agents or providing more passageways through the coating (col. 11).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Alberts or Cheng and Oshlack since Oshlack provides the guidance for formulating once a day controlled release devices for a therapeutic effect for 12 to 24 hours. One would be motivated to do so since Alberts/Cheng teach the advantages of formulating the instant HMG-CoA inhibitor in a once a day controlled release device. It is further the examiner's position and in the

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absence of unexpected results that Oshlack provides the general guidance is formulating a controlled release and depending on the drug, the Cmax will change according to the needed therapeutic dosage; this dosage is taught by Alberts and Cheng.

**Claims 1-13, 18-19, 21-22, 25-29, 31-54, 57-71, and 76-81 are rejected under 35 U.S.C. 103(a) as being unpatentable over Alberts et al (4,997,658) or Cheng et al (Pharmaceutical Research) in view of Sako et al (6,436,441).**

Alberts teaches a method of lowering plasma cholesterol levels. The method includes administering to a subject a time-controlled drug-delivery device containing an HMG-CoA reductase inhibitor (lovastatin). Alberts discloses that using a sustained or controlled release provides for a single dose to yield an equivalent or improved effect while lowering the peak drug plasma levels (col. 1, lines 39-50). By lowering the amount of plasma concentration in the blood, the potential side effects of the drug are reduced. The controlled release is over a 6 to 24 hour period (col. 2, line 63). Alberts discloses that this controlled release can be achieved by a variety of procedures known to those skilled in the art. The procedures suitable for the invention are diffusion-controlled systems, osmotic devices, dissolution controlled matrices, and erodible/degradable matrices (col. 3, lines 1-2).

Cheng et al teach the efficacy of a sustained/controlled release dosage form for the delivery of lovastatin or simvastatin. Cheng et al teach lowering cholesterol level. Cheng teaches the lower plasma concentrations of the instant drugs results in equal or better therapeutic efficacy. The instant Cmax is taught (figures).

Alberts or Cheng et al do not specify the formulation for the control release device.

Sako et al teaches a sustained release hydrogel formulation. Sako teaches using polymer weights to manipulate the release rates of the drug (Figures). Further Sako teaches manipulating the pharmacokinetic parameters to yield the desired effect (col. 5 and examples). Lastly, Sako teaches hyperlipemia agents such as pravastatin are suitable for the invention (col. 3, line 4). The reference teaches a once a day formulation for a 24-hour therapeutic release.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Alberts or Cheng and Sako et al since Sako provides the guidance for formulating once a day controlled release devices for a therapeutic effect for 24 hours. One would be motivated to do so since Alberts/Cheng teach the advantages of formulating the instant HMG-CoA inhibitor in a once a day controlled release device. It is further the examiner's position and in the absence of unexpected results that since Sako provides the general guidance for formulating a controlled release, the corresponding values would depend on the drug of choice; these values are taught by Albert and Cheng.

### ***Response to Arguments***

Applicant argues that the only information in Alberts et al directed towards the in-vivo performance of the formulation is in example 2. It is argued however that the formulation is administered to dogs and not humans. Applicant argues that Cheng et al also is directed towards dogs. Applicant argues that the dog data in the reference are

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not instructive with respect to performance of these formulations in humans. In regards to the method claims, since the prior art teaches the Tmax ranges and in-vivo results, the applicant needs to address the assertion of the difference between dog data and human data.

Applicant's arguments have been fully considered but they are not persuasive. Firstly, Cheng et al state that "the dog may not be a good model for predicting relative bioavailability of lovastatin or simvastatin" and this is by no means is a conclusive statement that the dog data is not instructive with respect to humans since Cheng clearly states "may not." Without data, applicant's argument does not have substantial weight.

Secondly, applicant's has argued functional limitations in composition claims, which are viewed as intended use since applicant is limiting the claim to what happens in-vivo after consumption of the product rather than limiting the product itself. If applicant contends there is a marked difference between the prior art's release and instant invention's, then applicant must provide evidence in a Rule 132 Declaration. As recognized by the applicant, Alberts teaches a method of HMG-CoA Reductase utilizing a drug delivery device for a controlled release of the drug into an environment of use. The inventive claims are directed towards a controlled release oral solid dosage of HMG-CoA Reductase. Although applicant has claimed a functional limitation, the applicant has not shown how the instant claims are distinguishable over the prior art. The examiner's arguments above also hold true for the Cheng reference. Further, it is pointed out that Cheng teaches the administration in dog and human models and also

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teach a sustained/controlled release device. Again, applicant has not distinguished the inventive claims over the prior art.

Applicant argues that Oshlack is directed towards a controlled release formulation having a coat derived from an aqueous dispersion of a hydrophobic polymer. It is argued that Oshlack only teaches in-vivo data directed towards opioid analgesics which are different from instant actives. Applicant argues that Sako et al is directed towards a hydrogel sustained release device and none of the examples include instant active.

Applicant's arguments have been fully considered but they are not persuasive. The examiner points out that the primary references do teach controlled release device, as also recognized by the applicant in the arguments presented. However, as stated in the rejection, the references do not specify the controlled release formulation. Therefore, the examiner relies on Oshlack and Sako to teach a controlled release formulation. Both Oshlack and Sako provide guidance in preparing a controlled release dosage and clearly state that these devices are suitable for various drugs without limitation. Oshlack provides the general guidance to manipulate the release rate and extend T<sub>max</sub> or shorten the time frame by adding release rate modifiers. In figure 16, Oshlack teaches a T<sub>max</sub> of 9 and applicant recites that T<sub>max</sub> is "about" ten hours. It is also noted that standard deviation would have the T<sub>max</sub> fall within the recited range. Furthermore, clearly the T<sub>max</sub> and plasma concentration will depend on the drug of choice and formulation.



Lastly, applicant is reminded that the claims are rejected under 103; thus neither reference standing alone has to anticipate the instant invention. The prior art together has to suggest inventive claims. Furthermore, the secondary reference does not have to teach all the limitations of the inventive claims since the broad aspect of the claims, i.e. the instant active and Tmax, are encompassed by the primary references.

### ***Conclusion***

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

### ***Correspondence***

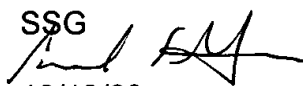
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sharmila S. Gollamudi whose telephone number is (703) 305-2147. The examiner can normally be reached on M-F (7:30-4:30).

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman Page can be reached on (703) 308-2927. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

SSG

  
10/13/03

  
MICHAEL G. HARTLEY  
PRIMARY EXAMINER